Fibrosis and Cirrhosis of the Liver

Basics

OVERVIEW
- The liver is the largest gland in the body; it has many functions, including production of bile (a fluid substance involved in digestion of fats); bile ducts begin within the liver itself as tiny channels to transport bile—the ducts join together to form larger bile ducts and finally enter the extrahepatic or common bile duct, which empties into the upper small intestine; the system of bile ducts is known as the “biliary tree”
- The gallbladder is the storage unit for bile; bile is stored until it is needed for fat digestion
- “Fibrosis of the liver” involves the formation of scar tissue that replaces normal liver tissue
- “Cirrhosis of the liver” is generalized (diffuse) formation of scar tissue (fibrosis), associated with regenerative nodules and deranged liver architecture

GENETICS
- Familial (runs in certain families or lines of pets) susceptibility for long-term (chronic) inflammation of the liver (condition known as “chronic hepatitis”)—Doberman pinschers, cocker spaniels, Labrador retrievers

SIGNALMENT/DESCRIPTION OF PET
Species
- Dogs
- Cats
Breed Predilections
- Any breed or mixed-breed dog
- Copper-storage liver disease (known as “copper-storage hepatopathy”)—Bedlington terriers, Dalmatians, possibly some Doberman pinschers, Labrador retrievers
- Scarring of the liver in young dogs of unknown cause (so-called “juvenile idiopathic hepatic fibrosis”)—German shepherd dogs, standard poodles
- Uncertain disorders—West Highland white terriers, Skye terriers
- Cats—long-term [chronic] inflammation of the bile duct or biliary tree (known as “cholangitis”) and inflammation of the bile ducts and liver (known as “cholangiohepatitis”) leading to blockage of the extrahepatic or common bile duct (extrahepatic bile duct obstruction) may develop progressive damage and scarring of the biliary tree and liver (known as “biliary cirrhosis”)

Mean Age and Range
• Cirrhosis (dogs)—any age; common in middle to old age
• Copper-storage liver disease (copper-storage hepatopathy) and scarring of the liver of unknown cause (idiopathic hepatic fibrosis)—young/middle-aged adults
• Progressive damage and scarring of the biliary tree and liver (biliary cirrhosis) in cats with long-term (chronic) inflammation of the bile ducts and liver (cholangiohepatitis)—greater than 7 years of age

Predominant Sex
• Cocker spaniels—males are 2–8 times more likely to develop fibrosis and cirrhosis of the liver than females
• Doberman pinschers and Labrador retrievers—may be more common in females than in males

SIGNS/OBSERVED CHANGES IN THE PET
• Initially—vague and non-specific signs
• Later—relate to complications of increased blood pressure within the portal vein (the vein carrying blood from the digestive organs to the liver; condition known as “portal hypertension”) and to impaired liver function; signs include nervous system signs (such as seizures, blindness) caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia (known as “hepatic encephalopathy”); fluid buildup in the abdomen (known as “ascites”); bleeding in the stomach and/or upper small intestine
• Long-term (chronic) intermittent sluggishness (lethargy), lack of appetite (known as “anorexia”), reduced or poor body condition
• Gastrointestinal signs: vomiting, diarrhea or constipation
• Black, tarry stools due to the presence of digested blood (known as “melena”): late stage of disease
• Increased thirst (known as “polydipsia”) and increased urination (known as “polyuria”)
• Late onset—fluid buildup in the abdomen (ascites); yellowish discoloration to the gums and other tissues of the body (known as “jaundice” or “icterus”); bleeding; nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia (hepatic encephalopathy)
• Cats—fluid buildup in the abdomen (ascites) uncommon; drooling (known as “ptyalism”) with nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia (hepatic encephalopathy)
• Liver size—small liver size in dogs; variable liver size in cats
• Bleeding tendencies (uncommon)
• Skin lesions with superficial, ulcerative inflammation (known as “superficial necrolytic dermatitis”)—not true cirrhosis

CAUSES
• Long-term (chronic) liver injury
• Long-term (chronic) inflammatory bowel disease (IBD)
• Inflammation of the pancreas (known as “pancreatitis”)
• Drug- or toxin-induced liver injury—copper-storage liver disease (copper-storage hepatopathy); medications to control seizures (known as “anticonvulsants”);azole medications to treat fungal infections; medication to treat intestinal parasites (oxibendazole); antibiotic (trimethoprim-sulfamethoxazole); nonsteroidal anti-inflammatory drugs (NSAIDs); long-term (chronic) food borne toxin (aflatoxins)
• Infections—leptospirosis, canine adenovirus-1 infection
• Long-term (chronic) inflammation of the bile ducts and liver (known as “cholangiohepatitis”) in cats
• Long-term (chronic) blockage of the extrahepatic or common bile duct (extrahepatic bile duct obstruction)—lasting more than 6 weeks—in dogs or cats
• Single episode of massive tissue death in the liver (known as “hepatic necrosis”)

RISK FACTORS
• Breed predisposition: copper toxicity to liver cells (known as “hepatotoxicity”) or other causes yet ill-defined
• Excessive intake of copper from the diet; accumulation of copper or iron in the liver
• Long-term (chronic) inflammation of the liver and bile ducts
• Blockage of the extrahepatic or common bile duct (extrahepatic bile duct obstruction)
• Long-term (chronic) administration of phenobarbital (medication to control seizures) in dogs
**Treatment**

**HEALTH CARE**
- Outpatient—pets with minimal signs
- Inpatient—diagnostic tests; treatment for dehydration, lack of appetite (anorexia), severe hepatic encephalopathy, or bleeding in the intestines due to blood vessel disease caused by high blood pressure (known as “hypertensive vasculopathy”)
- Fluids
- B-complex vitamins (especially for cats); vitamin K1
- Glucose—if pet has low blood sugar (known as “hypoglycemia”)
- Potassium chloride—in fluids, as needed
- Tap the abdomen and remove excess fluid (procedure known as “abdominocentesis”) as treatment for tense abdomen, causing signs (such as difficulty breathing); used in cases that do not respond to medical treatments to remove the excess fluid

**ACTIVITY**
- Limit activity

**DIET**
- Withhold food in cases of sudden (acute), severe hepatic encephalopathy (such as those with stupor or coma) or vomiting associated with intestinal bleeding or inflammation of the pancreas (pancreatitis); consider providing nutrition intravenously (known as “parenteral nutrition”)
- Hepatic encephalopathy (nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia): restrict protein intake, use soy or dairy protein sources (dogs) combined with medical treatment to increase nitrogen tolerance; individualize protein intake (maintain body condition, maintain albumin [type of protein] levels, control hepatic encephalopathy)
- Sodium restriction if the pet has fluid buildup in the abdomen (ascites)
- Fat restriction rarely needed
- Supplement water-soluble vitamins (such as vitamin B)

**SURGERY**
- Cirrhosis—high anesthetic risks; gas anesthetics preferred— Isoflurane or sevoflurane
- Blood-clotting disorder (known as “coagulopathy”)—increased likelihood of bleeding, with even minor surgeries
- Postoperative intensive care—critical to avoid hepatic encephalopathy (nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia), maintain hydration and normal blood sugar
- Susceptible to movement of intestinal bacteria into the body—administer appropriate antibiotics

**Medications**
Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive
- Treatments for specific etiologies: chelate copper if the pet has copper-storage liver disease: to “chelate copper” is to use specific chemicals to tie up copper in the system and to allow it to be removed from the body
- Discontinue medications that potentially may be toxic to the liver, as directed by your pet’s veterinarian
- Long-term inflammation of the liver (chronic hepatitis)—medications to alter the immune response (known as “immune modulation”): steroids (prednisolone, prednisone); azathioprine (a chemotherapeutic drug used to decrease the immune response) in dogs (may be used in combination with prednisone, antioxidants [such as S-adenosylmethionine or SAMe, vitamin E], and medication to decrease scarring of the liver [known as “antifibrotics,” such as ursodiol, polyunsaturated polyenylphosphatidylcholine, colchicine])
- Medications to protect the liver—ursodeoxycholate, vitamin E, SAMe; elemental zinc
- Medications to protect the lining of the stomach
- Medications to eliminate intestinal parasites
Medications to remove excess fluid from the body (known as “diuretics”) may be used in pets with fluid buildup in the abdomen (ascites)—furosemide, spironolactone. Dexamethasone is a steroid that may be used in pets with fluid buildup in the abdomen (ascites) instead of prednisone. Mycophenolate is a potential alternative for azathioprine.

Follow-Up Care

Patient Monitoring

- Bloodwork (including liver enzymes, albumin, blood urea nitrogen, cholesterol)—monthly or quarterly, depends on status of the pet
- Serial monitoring of total serum bile acids (bile acid levels are used to monitor liver function)
- Body condition score (estimate of weight status [under or overweight] as compared to normal weight) and muscle mass—reflects nutritional adequacy/nitrogen balance
- Monitor size of the abdomen: reflects volume of fluid buildup in the abdomen (ascites)
- Pets treated with azathioprine, mycophenolate or colchicine—monitor for possible bone-marrow toxicity using frequent complete blood counts (CBCs)

Preventions and Avoidance

- Reduce factors that may increase the likelihood of hepatic encephalopathy (nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia)—dehydration; infection; breakdown of lean muscle mass and body tissues (known as “catabolism”); low blood potassium (known as “hypokalemia”); high-protein meals; intestinal parasites; bleeding in the intestines; certain drugs

Possible Complications

- Hepatic encephalopathy (nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia), generalized disease caused by the spread of bacteria in the blood (known as “septicemia” or “blood poisoning”), bleeding—may be life-threatening
- Blood-clotting disorder (known as disseminated intravascular coagulopathy” or DIC)—may be a terminal event
- Death

Expected Course and Prognosis

- Occasional flare-ups of hepatic encephalopathy (nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia) and fluid buildup in the abdomen (ascites) may require hospitalization for adjustment of diet and medical treatment; sodium restriction and medications to remove excess fluid from the body (diuretics) may require titration to achieve optimal control of fluid buildup in the abdomen (ascites)
- Course of fibrotic/cirrhotic liver disease in dogs is poorly characterized. Scarring of the liver in young dogs of unknown cause (so-called “juvenile idiopathic hepatic fibrosis”) in dogs—survival up to 9 years following diagnosis
- Cirrhosis—survival greater than 5 years with careful medical treatment

Key Points

- “Fibrosis of the liver” involves the formation of scar tissue that replaces normal liver tissue
- “Cirrhosis of the liver” is generalized (diffuse) formation of scar tissue (fibrosis), associated with regenerative nodules and deranged liver architecture
- Treatment is designed to control signs and improve the pet’s condition, but not to cure (known as “palliative treatment”)
- Reduce factors that may increase the likelihood of hepatic encephalopathy (nervous system disorder caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia)—dehydration; infection; breakdown of lean muscle mass and body tissues (catabolism); low blood potassium (hypokalemia); high-protein meals; intestinal parasites; bleeding in the intestines; certain drugs